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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/250,083	02/15/1999	ANDREA DESSEN	GFN-5341	1676

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	31

DATE MAILED: 06/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/250,083	DESSEN ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,30 and 31* is/are rejected.

7)☒ Claim(s) *21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and objections not reiterated below are hereby withdrawn. Claims 21-22, 30, and 31 are pending.

Sequence Rules

The sequence rules have been complied with the CRF has been entered.

Claim Objections

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 depends from claim 20, which is cancelled. As claim 21 does not recite a method or product per se, and depends from a cancelled claim, it will not be further treated on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments with respect to claim 22 have been considered but are moot in view of the new ground(s) of rejection.

Claims 22, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK OR WRITTEN DESCRIPTION rejection.

Amended claim 22 recites a method of identifying an inhibitor of $cPLA_2$, wherein the inhibitor is provided and is limited to be one which interacts with one or more recited atoms in "the $cPLA_2$ active site." The specification discloses, on pages 7-9, methods of identifying an inhibitor of $cPLA_2$ by first designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the active site, or with one or more atoms of a disclosed list of amino acids, or with one or more amino acids in an electrostatic patch region, then synthesizing the potential inhibitor, and testing for inhibitory activity. The disclosure of the specification thus provides support for a general step of "providing" a potential inhibitor which interacts with the recited atoms in a method of identifying an inhibitor of $cPLA_2$; however, the specification does not disclose any particular compound (potential inhibitor) which is known to interact with the recited atoms/amino acids. The specification does not disclose how to design and/or synthesize such an inhibitor (see below), nor does the specification describe; e.g. by structure or sequence, any inhibitor designed to interact with the disclosed amino acids. The specification does not disclose a class of inhibitors known to interact with the recited amino acids. The specification does provide, on pages 39-42, working

examples of testing for inhibition of $cPLA_2$, however, the working examples teach only "adding" an inhibitor, but do not identify or otherwise describe the inhibitors used. As the specification fails to disclose specific compounds, or a class of compounds, or steps to design a compound which interacts with the claimed amino acid atoms, and fails to disclose any other information which would allow one skilled in the art to ascertain whether applicants did possess, or had actually designed inhibitors with the claimed properties, at the time of filing of the instant application, the specification fails to provide a complete description of the claimed invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 30 limits the activity to be inhibited in the method of claim 22 to lipid binding. The originally filed claims did not limit the activity of $cPLA_2$. The originally filed specification discloses, on page 8, methods for identifying inhibitors of $cPLA_2$ membrane binding, and on page 14 discloses that at least on region of $cPLA_2$ may bind a phospholipid substrate. While membrane binding may comprise lipid binding, the original specification does not disclose this. That the two activities are recited in different claims implies that applicant considered them to be separate or different activities. The working examples on pages 39-42 of the originally filed specification

disclose measurement of lipid cleavage, and inhibition thereof. Although cleavage of a lipid by an enzyme presumably involves binding between the lipid and the enzyme, binding and cleavage are not necessarily mutual events. A method of identifying an inhibitor of cleavage does not necessarily identify an inhibitor of binding. The original specification does not teach a method of detecting, measuring and/or inhibiting lipid binding to $cPLA_2$, and therefore does not teach a method of identifying an inhibitor of lipid binding. As applicant does not point to support in the original specification or claims for the newly claimed limitation of claim 30, and none is apparent, as set forth above, claim 30 recites new matter.

Claims 22, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The claims are not enabled because neither the specification nor the prior art teach how to identify an inhibitor of $cPLA_2$ using a potential inhibitor having the claimed properties. Amended claim 22 recites a method of identifying an inhibitor of $cPLA_2$, wherein the inhibitor is provided and is limited to be one which interacts with one or

more recited atoms in "the $cPLA_2$ active site." The specification discloses, on pages 7-9, methods of identifying an inhibitor of $cPLA_2$ by first designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the active site, or with one or more atoms of a disclosed list of amino acids, or with one or more amino acids in an electrostatic patch region, then synthesizing the potential inhibitor, and testing for inhibitory activity. However, the specification does not disclose how to design and/or synthesize such an inhibitor. The claims are not limited to "provide" only designed compounds; any compound with the claimed properties may be provided. The specification teaches, on page 9, that "study of the interaction of the candidate species with the model (of $cPLA_2$) can be performed using available software platforms" and lists several programs. This, however, is a teaching for using the "candidate species" once they are provided. This is not a teaching for how to determine whether a particular candidate compound is one which interacts with specific atoms of specific amino acids in the protein. The specification does not describe; e.g. by structure or sequence, any compound known to interact with "one or more: of the disclosed amino acids, nor does the specification disclose a class of inhibitors known to interact with one or more of the recited amino acids. The specification does provide, on pages 39-42, working examples of testing for inhibition of $cPLA_2$, however, the working examples teach only "adding" an inhibitor, but do not identify or otherwise describe the inhibitors used. Many inhibitors of PLA_2 enzymes are known in the art (see e.g. GLASER et al. IDS ref: Adv. Pharm. (1995) vol. 32, pp. 31-66); however, the prior art does not teach that these compounds are known to interact with the recited atoms on the claimed amino acids.

The specification does not teach how to determine whether a provided compound interacts with the recited atoms/amino acids. While methods of determining binding to particular residues of a protein are generally known in the art, no such methods are taught by either the prior art of the instant specification to detect binding/interaction with specific atoms of the recited amino acids in $cPLA_2$. Methods to determine interaction of a candidate inhibitor with particular atoms of a protein usually requires crystallization of the enzyme/candidate complex. For any given complex, crystallization is unpredictable as each particular complex requires its own salt, temperature, etc. conditions for success. Crystallization of a $cPLA_2$/candidate complex under certain conditions does not predict success for crystallization of any other complex. The level of skill in the art of enzyme inhibition is acknowledged to be high. Despite this, given the lack of teaching in either the prior art or the instant specification for compounds (i.e. potential inhibitors) known to interact with the claimed atoms/amino acids of cPLA2, or for a method of designing such compounds with the claimed properties, or for methods of identifying compounds with the claimed properties, it would require undue experimentation by one skilled in the art to identify an inhibitor of $cPLA_2$ by providing a potential inhibitor which interacts with one or more of the claimed atoms on the recited amino acids. For these reasons, the claims are not enabled.

Conclusion

Claims 22, 30 and 31 are rejected; claim 21 is objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

mam
June 20, 2003